REMARKS

Claims 1-38 were pending the application. Claims 18-24 have been canceled, without prejudice, as being directed to a non-elected invention. Claims 2, 3, 30, 35, and 38 have also been canceled, and claims 1, 4-9, 15, 25, 29, and 34 and 36-37 have been amended. Accordingly, upon entry of this amendment, claims 1, 4-17, 25-29, and 31-34, 36, and 37 will be pending.

Support for the amendments to claims 1, 4-9, 15, 25, 29, and 35-37 may be found throughout the specification, including the originally filed claims.

Table 1 was also amended to correct a typographical error at page 1, line 6. The word "6-Phosphoglucolactonase" was replaced with the word "6-Phosphogluco**no**lactonase." The abstract has been amended to more clearly describe the disclosed subject matter. The title has also been amended to more clearly describe the claimed subject matter.

No new matter has been added. Any amendments to the claims was done solely to more particularly point out and distinctly claim the subject matter of Applicants' invention in order to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Priority

The Examiner has stated that

> [t]he instant application is granted the benefit of priority for the U.S. Provisional Application Nos. 60/141,031, filed on June 25, 1999, 60/143,208, filed on July 9, 1999, and 60/151,572, filed on August 31,1999, as requested in the declaration and the first lines of the specification. Acknowledgment is made of applicant's claim for foreign priority based on applications (27 total) filed in Germany. It is noted, however, that applicant has not filed certified copies of the German applications as required by 35 U.S.C. § 119(b).

Applicants respectfully submit that Applicants will provide certified copies of all of the German applications to which this application claims priority prior to issuance of the instant application.

Information Disclosure Statement

No information disclosure statement has been filed with the instant application as of the date mailed of the instant Office action. Applicants are reminded that they have a duty to disclose all information, of which they are aware, relevant to the patentability of the pending claims (see 37 C.F.R. § 1.56 and M.P.E.P. § 2000).

Applicants respectfully submit that an Information Disclosure Statement is being filed concurrently herewith.

Objections to the Specification

The Examiner is of the opinion that "[i]in the specification, the Abstract is objected to for not completely describing the disclosed subject matter...The Examiner suggests the inclusion of the definition of "SMP" for completeness."

Applicants respectfully traverse the foregoing objection to the Abstract. However, in an effort to expedite prosecution of the application, Applicants have amended the abstract in a manner consistent with the Examiner's suggestion. Accordingly, reconsideration and withdrawal of the foregoing objection is requested.

The Examiner also states that "[t]he title is objected to for not adequately describing the claimed subject matter." The Examiner suggests the following new title: "Polynucleotides Encoding a 6-Phosphoglucolactonase from *Corynebacterium glutamicum*."

Applicants respectfully traverse the foregoing objection to the title. However, in an effort to expedite prosecution of the application, Applicants have amended the title as suggested by the Examiner. Accordingly, Applicants request reconsideration and withdrawal of the foregoing rejection.

The Examiner further states that "[t]he specification is objected to for missing Appendix A and Appendix B. These appendixes are referred to throughout the specification. In Applicant's transmittal letter from June 23, 2000, Appendix A is noted as containing 156 pages and Appendix B is noted as containing 52 pages. Applicants state that said appendixes

have been submitted; however, no appendixes are in the file." The Examiner is further of the opinion that

> since Applicants' provisional applications contain appendix data and since they are expressly incorporated by reference, Applicants can amend these appendixes into the specification by way of amendment in response to the instant Office action. ***Alternatively, Applicants can submit documentation to prove that Appendix A and Appendix B were submitted with the instant application on June 23, 2000 as noted in the transmittal to support their insertion. An amendment is required to include Appendix A and Appendix B in the file.*** [Emphasis Added].

Applicants respectfully submit that Appendix A and Appendix B were submitted together with the instant application on June 23, 2001. As evidence of the submission of Appendix A and Appendix B with the instant application on June 23, 2001, Applicants submit herewith a copy of the transmittal form which lists all of the items submitted with the instant application, including Appendix A and Appendix B, as well as a date-stamped return postcard, date-stamped by the U.S. Patent and Trademark Office on June 23, 2001, which lists all of the items submitted with the instant application, including Appendix A and Appendix B. Applicants have submitted herewith replacement copies of Appendix A and Appendix B.

The Examiner is further of the opinion that

> [t]he specification is objected to for being confusing in its description of SEQ ID NOs: 1/2 as described in Table 1. This open reading frame is described as having "6-phosphoglucolactonase" function. No definition of this enzymatic function is found in the art. The Examiner did find 6-phosphogluconolactonase (see attached result set form the Registry database). Appropriate clarification and, possibly, amendment to the specification is required. The Examiner notes that no explanation of the function listed in Table 1 had been disclosed at the time of filing. Therefore, it is wholly unclear whether the function is Table 1 is a typographical error or a novel function found in *C. glutamicum.*

Applicants respectfully submit that the misspelling of the word 6-Phosphogluconolactonase in Table 1 of Applicants specification was merely a

typographical error. As stated by the Examiner, the term 6-Phosphoglucolactonase is not known in the art to refer to any specific enzymatic function. Accordingly, it is clear that Applicants intended the term to read "6-Phosphogluco**no**lactonase." This term is known in the art to refer to a specific enzymatic function, and therefore, one of skill in the art would understand the intended meaning of the term to be "6-Phosphogluco**no**lactonase." Applicants have amended Table 1 to correct the typographical error. Accordingly, Applicants respectfully request reconsideration and withdrawal of the aforementioned objection.

Objections to the Claims

The Examiner has objected to claims 1-17 and 25-38 "for containing non-elected subject matter. All reference to SEQ ID NOs: 3/4, 5/6, 7/8, 9/10, 13/14, 15/16, 17/18, 19/20, and 21/22 must be deleted."

Applicants respectfully submits that the claims have been amended such that they refer only to SEQ ID NO:1 and SEQ ID NO:2. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

The Examiner has objected to claim 2 to under 37 C.F.R. § 1.75(c), as being, according to the Examiner, "of improper dependent form for failing to further limit the subject matter of a previous claim." In particular, the Examiner is of the opinion that "[t]he further limitation added in Claim 2 is an inherent feature in the subject matter of Claim 1 since all the genes in Table 1 are disclosed as encoding SMP polypeptides."

Applicants respectfully traverse the foregoing objection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claim 2 has been canceled thereby obviating the Examiner's rejection. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

The Examiner has objected to claims 15 and 30 under 37 C.F.R. § 1.75(c), "as being of improper dependent form for failing to further limit the subject matter of a previous claim." In particular, the Examiner is of the opinion that "[b]ecause of the breadth of the term 'modulation' and since expression of 6-phosphogluconolactonase will affect the production of chemicals in the host cells, this 'modulation' limitation does not further limit the subject matter of the parent claim effectively."

Applicants respectfully traverse the foregoing objection. However, in the interest of expediting prosecution and in no way acquiescing to the Examiner's objection, Applicants have canceled claim 30 and amended claim 15 such that it no longer refer to "modulation" of production of a fine chemical. As amended, claim 15 is directed to the host cell of claim 12, wherein the expression of said nucleic acid molecule results in the production of a fine chemical. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing objection to the claims.

Rejection of Claims 2, 8, and 34 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 2, 8, and 34 are rejected under 35 U.S.C. § 112, second paragraph, as being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that "[t]he abbreviation "SMP" is used in Claim 2 without appropriate definition upon its first appearance in the claims. The Examiner suggests replacing 'SMP polypeptide' with -sugar metabolism and oxidative phosphorylation (SMP) polypeptide-."

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claim 2 has been canceled thereby obviating the Examiner's rejection. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 8 and 34 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 8 and 34 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that "[i]n Claim 8, the term "stringent conditions" in reference to hybridization conditions is unclear. On page 28 of the instant specification, preferred embodiments are described for "stringent conditions" but a precise definition is not clear."

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution and in no way acquiescing to the Examiner's rejection, Applicants have amended claim 8 such that the claim recites specific hybridization conditions. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 25-33 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 25-33 under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that "[t]he reference to the 'vector of claim 12' is improper since Claim 12 is drawn to a host cell. The appropriate claim would seem to be Claim 11. The instant claims will be examined as is Claim 25 depends from Claim 11."

Applicants have amended claim 25 such that it is dependent on claim 11. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claim 29 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claim 29 under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that

[t]he various genus/species names are unclear for the following reasons:
a) *"Corynebacterium, lilium"* should not be separated by a comma.
b) *"Brevibacterium parrqffinofyticum"* is misspelled and should be —parrafinoliticum—.
c) *Brevibacterium divaricatum* and *Brevibacterium lactofermentum* are synonyms of *Corynebacterium glutamicum* (see attachment) and are inappropriate alternatives in a Markush group whose members must all be distinct.
d) *Brevibacterium healii, Brevibacterium ketoglutamicum, and Brevibacterium paraffinoliticum* are synonyms of *Rhodococcus erythropolis* (see attachment) and are inappropriate alternatives in a Markush group whose members must all be distinct. All but one of the three noted must be removed.
e) *Corynebacterium acetoglutamicum, Corynebacterium fujiokense, Corynebacterium nitrilophilus,* and *Corynebacterium butanicum* are unknown genus/species organisms.

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claim 29 has been amended to delete the comma separating *Corynebacterium lilium.* The spelling of *Brevibacterium parrafinoliticum* has also been corrected. *Brevibacterium divaricatum* and *Brevibacterium lactofermentum* have been deleted from the claim. *Brevibacterium healii* and *Brevibacterium ketoglutamicum* have also been deleted from the claim.

With respect to subsection (e) of the Examiner's comments, Applicants respectfully submit that *Corynebacterium acetoglutamicum, Corynebacterium fujiokense,* and *Corynebacterium nitrilophilus,* are all known in the art. The term *Corynebacterium acetoglutamicum* is discussed in U.S. Patent No. 5,766,925 (see column 11, line 20), which is attached hereto as Appendix C. The term *Corynebacterium fujiokense* is discussed in U.S. Patent No. 5,840,548, which is attached hereto as Appendix D (see column 1, line 52). The term *Corynebacterium nitrilophilus* is discussed in U.S. Patent No. 5,508,181, which is attached hereto as Appendix E (see column 4, line 25). The term *Corynebacterium butanicum* has been deleted from claim 29. Accordingly, in light of the foregoing, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, second paragraph rejection.

Rejection of Claim 38 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claim 38 under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that "[t]he term 'regulatory region' of the gene that encodes SEQ ID NO: 2, described as SEQ ID NO: 1, is wholly unclear. No promoter or enhancer region is described in the specification or the art; these are typical regulatory regions."

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claim 38 has been canceled thereby obviating the Examiner's rejection. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 5-8 and 34 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 5-8 and 34 under 35 U.S.C. § 112, first paragraph, written description, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." In particular, the Examiner is of the opinion that

> [n]one of these claims include a function with the claimed structure....The instant specification discloses DNAs relating to SEQ ID NOs: 1/2 encoding polypeptides that function as 6-phosphoglucolactonases (see specification objection above concerning enzyme name and function in Table 1). Applicants have fully described the genus relating to said SEQ ID NOs with both sequence identity limitations and functional limitations (i.e., having 6-phosphoglucolactonases function). However, the genus of the instant claims also contains polynucleotides within the sequence identity limitations, but having different function. Applicants have not fully described a genus that has sequence identity limitations in the absence of functional limitations. The Examiner suggests the insertion of a functional limitation on the polynucleotides in the genus of Claims 5-

> 7. However, due to the confusion of the function as noted above in the objection to the specification concerning the possible typographical error in Table 1, the assignment of a clear function to SEQ ID NO:1 and DNAs encoding SEQ ID NO:2 may be problematic since said function requires support in the specification as originally filed.

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claims 5 and 6 have been amended such that a functional limitation has been introduced, as suggested by the Examiner. Accordingly, Applicants respectfully submit that based on the teachings in Applicants' specification, the invention claimed in claims 5 and 6 is adequately described.

With respect to claim 7, Applicants respectfully submit that claim 7 is directed to isolated nucleic acid molecules comprising fragments of SEQ ID NO:1 of a specific number of nucleotides. In Example 15 of the *Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. §112, First Paragraph Written Description Requirement* the "theoretical specification" discloses a messenger RNA sequence, SEQ ID NO:1, which encodes a human growth hormone. The "theoretical specification" claims antisense molecules that inhibit the production of human growth hormone. The Guidelines provide that

> [c]onsidering the specification's disclosure of (1) ***the sequence (SEQ ID NO:1) which defines and limits the structure of any effective molecules such that one skilled in the art would be able to immediately envisage members of the genus embraced by the claim*** and 2) the functional characteristics of the claimed invention as well as a routine art-recognized method of screening for antisense molecules which provide further distinguishing characteristics of the claimed invention, along with, 3) the general level of knowledge and skill in the art, one skilled in the art would conclude that applicant was in possession of the invention.....***the claimed invention is adequately described. (Emphasis added).***

Similar to Example 15 of the *Interim Guidelines*, the instant specification describes the nucleotide sequence of the nucleic acid molecules of the invention (SEQ ID NO:1) ***which define and limit the structure of any nucleotide fragments such that one***

skilled in the art would be able to immediately envisage members of the genus embraced by the nucleotide fragment claims. Thus, based on the *Written Description* guidelines, the invention claimed in claim 7 is adequately described. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the foregoing rejection as it pertains to claims 5-8 and 34.

Rejection of Claims 36 and 37 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 36 and 37 under 35 U.S.C. § 112, first paragraph, written description, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." In particular, the Examiner is of the opinion that

> [c]laims 36 and 37 are drawn to host cells containing modified DNA, by disruption or modification, related to SEQ ID NO:1. None of these claims include a function with the claimed structure. The instant specification discloses DNAs relating to SEQ ID NOs: 1/2 encoding polypeptides that function as 6-phosphoglucolactonases (see specification objection above concerning enzyme name and function in Table 1). Applicants have fully described the genus relating to said SEQ ID NOs with both sequence identity limitations and functional limitations (i.e., having 6-phosphoglucolactonases function). However, the genus of the instant claims also contains polynucleotides within the sequence identity limitations, but having different function. Applicants have not fully described a genus that has sequence identity limitations in the absence of functional limitations.

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claims 36 and 37 have been amended such that they recite a function of the claimed nucleic acid molecule. Applicants respectfully submit that claims 36 and 37, as amended, are adequately described by Applicants' specification. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claim 38 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claim 38 under 35 U.S.C. § 112, first paragraph, written description, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention."

In particular, the Examiner is of the opinion that

> [c]laim 38 is drawn to a host cell comprising SEQ ID NO: 1 with a modified regulatory region. This claim does not include a function with the claimed structure....The instant specification discloses DNAs relating to SEQ ID NOs:l/2 encoding polypeptides that function as 6-phosphoglucolactonases (see specification objection above concerning enzyme name and function in Table 1). Applicants have fully described the genus relating to said SEQ ID NOs with both sequence identity limitations and functional limitations (i.e., having 6-phosphoglucolactonases function). However, the genus of the instant claims also contains polynucleotides within the sequence identity limitations, but having different function. Applicants have not fully described a genus that has sequence identity limitations in the absence of functional limitations.

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claim 38 has been canceled thereby obviating the Examiner's rejection. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 6-8 and 34 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 6-8 and 34 under 35 U.S.C. § 112, first paragraph, because, according to the Examiner, "the specification, ***while being enabling for polynucleotides with at least, for example, 90% sequence identity to a polynucleotide which encodes SEQ ID NO:2***, does not reasonably provide enablement for polynucleotides with such low sequence identity, such as the 50% identity claimed or the 15-mer fragment claimed using comprising language." [emphasis added].

In particular, the Examiner is of the opinion that

> [t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The amount of experimentation required of one of skill in the art to use the claimed invention to the full extent of its scope is undue....Applicants present no guidance or working examples of the use of polynucleotides that have such low sequence identity with respect to SEQ ID NO: 1. The nature of the invention is such that the DNA encodes a functional protein, a 6-phosphoglucolactonase useful in promoting fine chemical biosynthesis in *C. glutamicum,* and with such a great deviation from the known sequence, the predictability of functionality becomes extremely low. Such enormous breadth and unpredictability renders the instant claims not enabled to the foil extent of their scope without undue experimentation.

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claim 6 has been amended such that it is directed to a nucleic acid molecule comprising a nucleotide sequence which has at least 90% identity with the nucleotide sequence of SEQ ID NO:1. Furthermore, claim 5 have been amended such that it is directed to isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a *Corynebacterium glutamicum* polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the nucleic acid molecule hybridizes to the complement of a nucleic acid molecule consisting of SEQ ID NO:1-in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C, and wherein said nucleic acid molecule encodes a polypeptide having 6-phosphogluconolactonase activity. The Examiner has expressly admitted that the specification is enabled for polynucleotides with at least 90% identical to SEQ ID NO:1. Accordingly, Applicants respectfully submit that Applicants' specification is clearly enabling with respect to claim 6, as amended.

With respect to claim 7, which is directed to nucleic acid molecules which comprise 15 contiguous nucleotides of SEQ ID NO:1, Applicants respectfully submit that one of ordinary skill in the art would be able to make and use the invention claimed in claim 7 using only routine experimentation. As set forth in the *Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. §112, First Paragraph Written Description Requirement*, because the claimed nucleotide sequence is defined and

limited, ***one skilled in the art would be able to immediately envisage members of the genus embraced by the nucleotide fragment claims***. Moreover, methods of generating fragments of the nucleic acid molecules of the present invention are well known in the art and also taught in Applicants' specification (*see,* for example, page 25, line 25 through page 27, line 19). Accordingly, one of ordinary skill in the art would easily be able to produce the claimed fragments without undue experimentation.

In summary, it is Applicants' position that, given the guidance in Applicants' specification and the teachings in the art at the time the invention was made, one of ordinary skill in the art would be able to practice the invention as claimed using no more than routine experimentation. Accordingly, Applicants respectfully requests reconsideration and withdrawal of the foregoing rejection.

Rejection of Claim 35 Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claim 35 under 35 U.S.C. § 112, first paragraph, enablement, "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." In particular, the Examiner is of the opinion that

> [c]laim 35 is drawn to diagnosing the presence or activity of C. *diphtheriae* using a screen utilizing a DNA from *C. glutamicum.* While it would be common in the art to screen for *C. glutamicum* presence with a DNA from *C. glutamicum,* one of skill in the art would be required to perform undue experimentation to (1) screen for *C. diphtheriae* or (2) screen for activity using DNA)....The specification provides no guidance or working examples of screening for *C. diphtheriae* presence using SEQ ID NO: 1. The nature of the invention is such that if C. *diphtheriae* has a 6-phosphogluconlactonase gene, it is unpredictable whether or not such a gene could be detected by SEQ ID NO: 1, a 6-phosphoglucolactonase gene from another species. The state of the prior art is such that genes from a specific species are commonly used to detect the presence of the species, in a host organism for example; however, detecting varying species is not typical practice. Moreover, a method using the claimed method steps cannot, without undue experimentation, detect the activity of any organism, either *C.*

glutamicum or *C. diphtheriae;* an enzyme activity, or some other assay, would be required to assay for activity.

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claim 35 has been canceled thereby obviating the Examiner's rejection. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 7 and 8 Under 35 U.S.C. §102

The Examiner has rejected claims 7 and 8 under 35 U.S.C. § 102(b) as being "anticipated by Marra *et al.* (GenBank Accession Number AA915356 (April, 1998) vz29z08.rl Soares_thymus_2NbMT *Mm musculus* cDNA clone)." In particular, the Examiner is of the opinion that "[t]he instant claims are drawn to nucleic acid molecules comprising a15-mer fragment of SEQ ID NO: 1. Marra *et al.* teach a 456 nucleotide mRNA whose nucleotides 386-366 are identical to SEQ ID NO:1 from 792-812 (see attached alignment)."

Applicant respectfully traverses the foregoing rejection. Applicant respectfully submits that for a prior art reference to anticipate in terms of 35 U.S.C. §102 a claimed invention, prior art must teach ***each and every element*** of the claimed invention. Lewmar Marine v. Barient 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987). An alignment of the entire 456 nucleotide sequence of Marra *et al.* and the entire 828 nucleotide sequence of SEQ ID NO:1 does not indicate that there are 15 contiguous nucleotides which are identical between Marra *et al.* and SEQ ID NO:1 (see alignment provided herewith as Appendix B). Therefore, Marra *et al.* fails to teach each and every element of claim 7, as amended. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the foregoing rejection.

Rjection of Claim 9 Under 35 U.S.C. §102

The Examiner has rejected claim 9 under 35 U.S.C. § 102(b) "as being anticipated by Ma *et al.* (Cloning and Characterization of the *Pseudomonas aeruginosa* zw/Gene Encoding Glucose-6-Phophate Dehydrogenase, an Enzymes Important in Resistance to Methyl Viologen (Paraquat) J. Bacteriol. (April, 1998) 180(7): 1741-1749)." In particular, the Examiner is of the opinion that

> [t]he instant claim[s] is drawn to a DNA that is a portion of SEQ ID NO: 1 connected to a sequence encoding a heterologous polypeptide. Ma *et al.* teach the zwf gene that is later renamed to the *Pseudomonas aeruginosa* pgl gene which is analgous to the devB gene for 6-phosphogluconolactonase. The gene taught by Ma *et al.* readily contains a portion of SEQ ID NO: 1, since no limitation on how small the portion can be is noted in the claims. And *zwf* encodes a heterologous polypeptide.

Applicants respectfully traverse the foregoing rejection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claim 9 has been amended such that it is no longer directed to "a portion" of SEQ ID NO:1. Therefore, claim 9 is not anticipated by Ma *et al.* Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Double Patenting

The Examiner has stated that "Applicant is advised that should Claim 1 be found allowable, Claims 2 and 3 will be objected to under 37 C.F.R. § 1.75 as being a substantial duplicate thereof." In particular, the Examiner is of the opinion that

> [w]hen two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See M.P.E.P. § 706.03(k). For Claim 2, the further limitation of

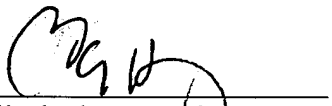
"SMP" polypeptides is contained in Claim 1 (see claim objection above for not further limiting the subject matter). For Claim 3, the fact that the DNAs are *C. glutamicum* in origin is also inherent in Claim 1 that is drawn to the exact sequence.

Applicants respectfully traverse the foregoing objection. However, in the interest of expediting prosecution and in no way conceding to the validity of the Examiner's position, claims 2 and 3 have been canceled thereby obviating the Examiner's rejection. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

SUMMARY

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,



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Dated: **October 22, 2002**

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

Please amend page 1, line 6 of Table 1, as follows:

--1 2 RXS02735 VV0074 14576 15280 6-Phosphogluconolactonase--

Please replace the title at page 1, line 1, with the following re-written title:

~~***CORYNEBACTERIUM GLUTAMICUM* GENES ENCODING PROTEINS INVOLVED IN CARBON METABOLISM AND ENERGY PRODUCTION~~

--POLYNUCLEOTIDES ENCODING A 6-PHOSPHOGLUCONOLACTONASE POLYPEPTIDE FROM *CORYNEBACTERIUM GLUTAMICUM*--

Please replace the title at page 69, line 1, with the following re-written title:

~~***CORYNEBACTERIUM GLUTAMICUM* GENES ENCODING PROTEINS INVOLVED IN CARBON METABOLISM AND ENERGY PRODUCTION~~

--POLYNUCLEOTIDES ENCODING A 6-PHOSPHOGLUCONOLACTONASE POLYPEPTIDE FROM *CORYNEBACTERIUM GLUTAMICUM*--

Please replace the abstract beginning at page 69, line 6, with the following re-written abstract:

--Isolated nucleic acid molecules, designated sugar metabolism and oxidative phosphorylation (SMP) nucleic acid molecules, which encode novel SMP proteins from *Corynebacterium glutamicum*, are described. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing SMP nucleic acid molecules, and host cells into which the expression vectors have been introduced. The invention still further provides isolated SMP proteins, mutated SMP proteins, fusion proteins, antigenic peptides and methods for the improvement of production of a desired compound from *C. glutamicum* based on genetic engineering of SMP genes in this organism.--

In the claims:

Please cancel claims 2, 3, 18-24, 30, 35, and 38 without prejudice, and amend claims 1, 4, 5, 6, 7, 8, 9, 15, 25, 29, and 34 and 36-37 as follows:

1. **(Amended)** An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, ~~SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, or SEQ ID NO:21,~~ or a complement thereof.

4. **(Amended)** An isolated nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2~~, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, or SEQ ID NO:22~~.

5. **(Amended)** An isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a *Corynebacterium glutamicum* polypeptide comprising the amino acid sequence of SEQ ID NO:2, ~~SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, or SEQ ID NO:22~~, wherein the nucleic acid molecule hybridizes to the complement of a nucleic acid molecule consisting of SEQ ID NO:1~~, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, or SEQ ID NO:21~~ in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C, and wherein said nucleic acid molecule encodes a polypeptide having 6-phosphogluconolactonase activity.

6. **(Amended)** An isolated nucleic acid molecule comprising a nucleotide sequence which has at least ~~50~~90% identity with the nucleotide sequence of SEQ ID NO:1, ~~SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, or SEQ ID NO:21,~~ wherein said nucleic acid molecule encodes a polypeptide having 6-phosphogluconolactonase activity, or the complement thereof.

7. **(Amended)** An isolated nucleic acid molecule comprising a fragment of at least 15 contiguous nucleotides of the nucleotide sequence of SEQ ID NO:1, ~~SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, or SEQ ID NO:21,~~ or the complement thereof.

8. **(Amended)** An isolated nucleic acid molecule which hybridizes to the nucleic acid molecule of any one of claims 1 and 4-7 ~~under stringent conditions~~ in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

9. **(Amended)** An isolated nucleic acid molecule comprising the nucleic acid molecule of any one of claims 1 and 4-7 ~~or a portion thereof~~ and a nucleotide sequence encoding a heterologous polypeptide.

15. **(Amended)** The host cell of claim 12, wherein the expression of said nucleic acid molecule results in the ~~modulation in~~ production of a fine chemical from said cell.

25. **(Amended)** A method for producing a fine chemical, comprising culturing a cell containing a vector of claim ~~12~~ 11, such that the fine chemical is produced.

29. **(Amended)** The method of claim 25, wherein said cell is selected from the group consisting of: *Corynebacterium glutamicum, Corynebacterium herculis, Corynebacterium~~,~~ lilium, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium acetophilum, Corynebacterium ammoniagenes, Corynebacterium fujiokense, Corynebacterium nitrilophilus, Brevibacterium ammoniagenes, ~~Brevibacterium butanicum, Brevibacterium divaricatum,~~ Brevibacterium flavum, Brevibacterium healii, Brevibacterium ketoglutamicum, Brevibacterium ketosoreductum, ~~Brevibacterium lactofermentum,~~ Brevibacterium linens, Brevibacterium ~~paraffinolyticum~~parafinoliticum,* and those strains set forth in Table 3.

34. **(Amended)** A method for producing a fine chemical, comprising culturing a cell whose genomic DNA has been altered by the inclusion of a nucleic acid molecule of any one of claims ~~1-9~~ 1 and 4-9.

36. **(Amended)** A host cell comprising the nucleic acid molecule of SEQ ID NO:1, ~~SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, or SEQ ID NO:21,~~ or the complement thereof, wherein the nucleic acid molecule is disrupted, and wherein said nucleic acid molecule encodes a polypeptide having 6-phosphogluconolactonase activity.

37. **(Amended)** A host cell comprising the nucleic acid molecule of SEQ ID NO:1, ~~SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, or SEQ ID NO:21,~~ or the complement thereof, wherein the nucleic acid molecule comprises one or more nucleic acid modifications, and wherein said nucleic acid molecule encodes a polypeptide having 6-phosphogluconolactonase activity.

APPENDIX A

1. An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, or a complement thereof.

4. An isolated nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2.

5. An isolated nucleic acid molecule which encodes a naturally occurring allelic variant of a *Corynebacterium glutamicum* polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the nucleic acid molecule hybridizes to the complement of a nucleic acid molecule consisting of SEQ ID NO:1, in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C, and wherein said nucleic acid molecule encodes a polypeptide having 6-phosphogluconolactonase activity.

6. An isolated nucleic acid molecule comprising a nucleotide sequence which has at least 90% identity with the nucleotide sequence of SEQ ID NO:1, wherein said nucleic acid molecule encodes a polypeptide having 6-phosphogluconolactonase activity, or the complement thereof.

7. An isolated nucleic acid molecule comprising a fragment of at least 15 contiguous nucleotides of the nucleotide sequence of SEQ ID NO:1, or the complement thereof.

8. An isolated nucleic acid molecule which hybridizes to the nucleic acid molecule of any one of claims 1 and 4-7 in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

9. An isolated nucleic acid molecule comprising the nucleic acid molecule of any one of claims 1 and 4-7 and a nucleotide sequence encoding a heterologous polypeptide.

10. A vector comprising the nucleic acid molecule of claim 1.

11. The vector of claim 10, which is an expression vector.

12. A host cell transfected with the expression vector of claim 11.

13. The host cell of claim 12, wherein said cell is a microorganism.

14. The host cell of claim 13, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium.*

15. The host cell of claim 12, wherein the expression of said nucleic acid molecule results in the production of a fine chemical from said cell.

16. The host cell of claim 15, wherein said fine chemical is selected from the group consisting of: organic acids, proteinogenic and nonproteinogenic amino acids, purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides, and enzymes.

17. A method of producing a polypeptide comprising culturing the host cell of claim 12 in an appropriate culture medium to, thereby, produce the polypeptide.

25. A method for producing a fine chemical, comprising culturing a cell containing a vector of claim 11 such that the fine chemical is produced.

26. The method of claim 25, wherein said method further comprises the step of recovering the fine chemical from said culture.

27. The method of claim 25, wherein said method further comprises the step of transfecting said cell with the vector of claim 11 to result in a cell containing said vector.

28. The method of claim 25, wherein said cell belongs to the genus *Corynebacterium* or *Brevibacterium.*

29. The method of claim 25, wherein said cell is selected from the group consisting of: *Corynebacterium glutamicum, Corynebacterium herculis, Corynebacterium lilium, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium acetophilum, Corynebacterium ammoniagenes, Corynebacterium fujiokense, Corynebacterium nitrilophilus, Brevibacterium ammoniagenes, Brevibacterium flavum, Brevibacterium healii, Brevibacterium ketoglutamicum, Brevibacterium ketosoreductum, Brevibacterium linens, Brevibacterium parafinoliticum,* and those strains set forth in Table 3.

31. The method of claim 25, wherein said fine chemical is selected from the group consisting of: organic acids, proteinogenic and nonproteinogenic amino acids, purine and pyrimidine bases, nucleosides, nucleotides, lipids, saturated and unsaturated fatty acids, diols, carbohydrates, aromatic compounds, vitamins, cofactors, polyketides, and enzymes.

32. The method of claim 25, wherein said fine chemical is an amino acid.

33. The method of claim 32, wherein said amino acid is drawn from the group consisting of: lysine, glutamate, glutamine, alanine, aspartate, glycine, serine, threonine, methionine, cysteine, valine, leucine, isoleucine, arginine, proline, histidine, tyrosine, phenylalanine, and tryptophan.

34. A method for producing a fine chemical, comprising culturing a cell whose genomic DNA has been altered by the inclusion of a nucleic acid molecule of any one of claims 1 and 4-9.

36. A host cell comprising the nucleic acid molecule of SEQ ID NO:1, or the complement thereof, wherein the nucleic acid molecule is disrupted, and wherein said nucleic acid molecule encodes a polypeptide having 6-phosphogluconolactonase activity.

37. A host cell comprising the nucleic acid molecule of SEQ ID NO:1, or the complement thereof, wherein the nucleic acid molecule comprises one or more nucleic acid modifications, and wherein said nucleic acid molecule encodes a polypeptide having 6-phosphogluconolactonase activity.

APPENDIX B

lalign output for aa915356 vs. SEQ ID NO 1

[ISREC-Server] Date: Wed Oct 16 23:14:12 MET 2002

```
reset matrix file to /export/molbio/share/fasta2/pam120.mat ./wwwtmp/lalign/.19246.1.seq : 456 aa
ALIGN calculates a global alignment of two sequences
 version 2.0uPlease cite: Myers and Miller, CABIOS (1989) 4:11-17
aa915356                                                456 aa vs.
SEQ ID NO 1                                             828 aa
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33.5% identity;         Global alignment score: -300

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              80        90                                       100
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                              110                                 120
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       :                   ::: ::::::                     :: ::: :
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                     130          140       150           160
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         :.:: .:      ::: ::::..: .  ::.:::: ::..: ..: :.     ::::.
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                   170          180                          190
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       :          :.: :    :::::.: ::::   ::.:              :::: : :
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                200                               210          220
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       ::     ::: :: ::::.:                     :::.   .:.:.:::::::.:
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```
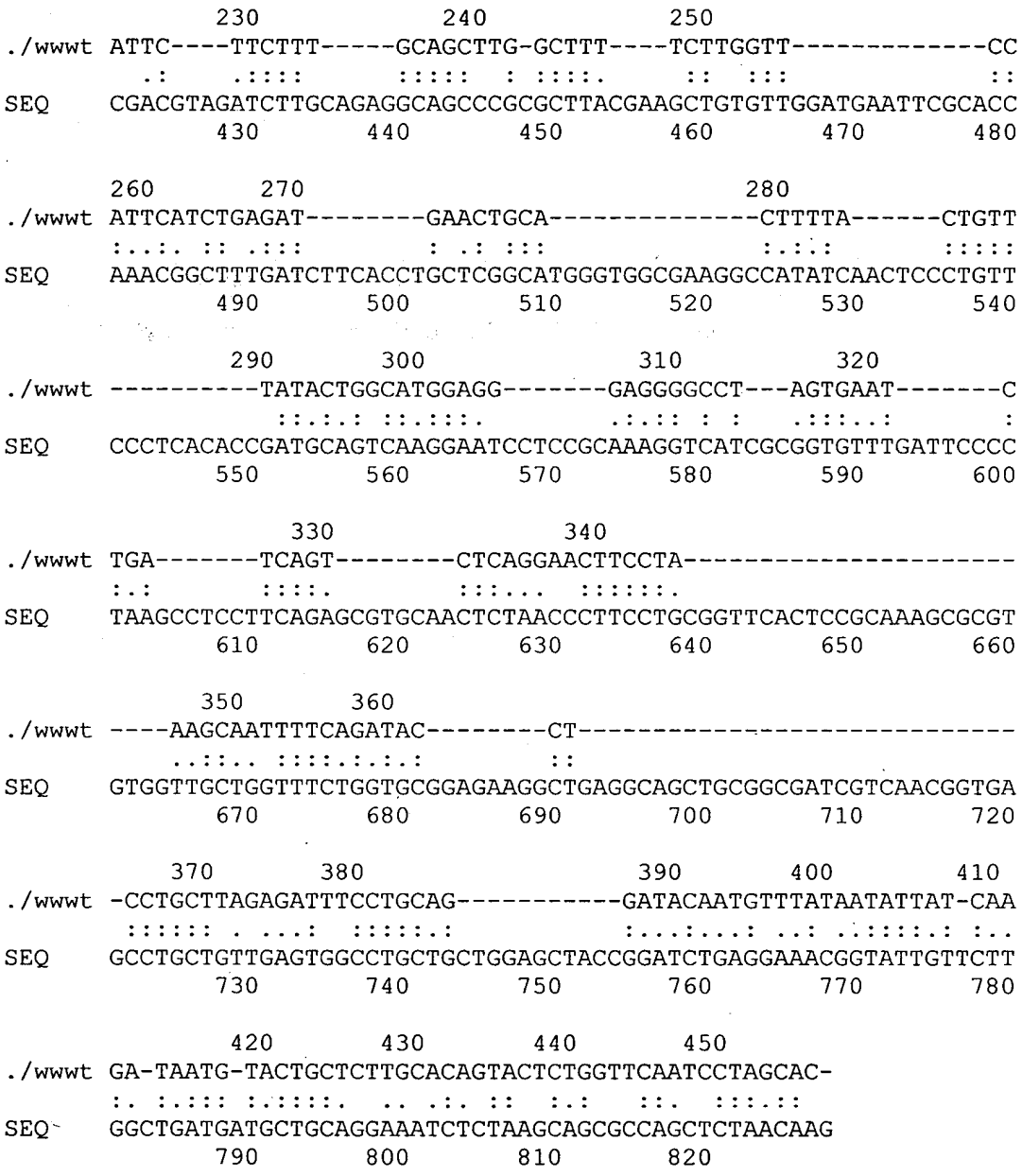

APPENDIX B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